

### **REMARKS**

Claims 1-39 are currently pending. Claims 33-39 have been withdrawn as being directed to non-elected subject matter. Claims 1-32 are rejected. Claims 1-7, 23 and 32 have been amended as described below. Support for this amendment is found, for example, page 8, lines 18-29; page 9, lines 20-30 through to page 10, lines 1-24. No new matter has been added by virtue of this amendment and entry is respectfully requested.

Applicants are herewith filing a 37 C.F.R. § 1.132 (herein referred to as a "Rule 132 declaration " attached as Exhibit A, signed by the inventor, Dr. Nancy Denslow. The declaration addresses the scope of enablement and the written description.

#### ***Claim Rejections Under 35 U.S.C. § 112- Scope of Enablement***

Claims 1-7 and 10-32 are rejected under 35 U.S.C. § 112, first paragraph. The Examiner asserts that the specification while being enabling for a method of detecting estrogenic or androgenic activity in a sample comprising sheepshead minnow or large mouth bass fish cells, the specification is not reasonably enabling for any type of fish species or detection of genes partially encoded. Applicants respectfully traverse.

Applicants describe the identification of genes whose expression is modulated with estrogen or androgen. These genes are identified by identifying, for example, the homologs in other fish species. Attached hereto, is a declaration by inventor Nancy Denslow. The declaration shows one methodology one of ordinary skill in the art could, without undue experimentation etc., identify the genes in other fish species based on the sequences identified in the specification. This methodology is one example that one of ordinary skill in the art could devise, based on the instant teachings to identify the genes induced by the estrogen or androgen. These genes will be identified as homologs in other species. The statement on the Method to Identify Homologous Sequences in other Fish Species (Exhibit "A") describes how one would find those homologs starting with the genes that were sequenced for largemouth bass and

sheepshead minnow. As shown in the example in Method to Identify Homologous Sequences in other Fish Species -- one of ordinary skill in the art can find the homologous genes in other species by either using the entire DNA segment in a BLAST search using the BLASTN program or the translated DNA segment that corresponds to the coding region of the gene in a BLASTP program. Both of these programs are freely available on the web from the NCBI.

The Examiner also asserts that:

it is unclear from the absence of evidence what part of the genes in each fish species provides correlative expression levels differences between a control and a cell acted on by an androgenic or estrogenic agent.

As explained by the Applicants in the Declaration attached hereto, “the entire sequence or any part of the sequence (at least 30 nucleotides in length) that is unique to the gene (or homolog) would provide correlative expression levels between control and exposed cells. Unique segments for genes can be determined by testing any segment via BLASTN to the entire genome sequence. A few segments may be specific for gene families (rather than the specific gene mentioned) and these segments would have lower correlative value – for example the DNA binding domain of all estrogen receptors (alpha, beta and gamma) is 95% identical – a sequence containing only this domain would not distinguish the three receptors from each other but would give an average value for their expression. In this case, all three of the receptors are up regulated by estrogen.”

In order to expedite prosecution, Applicants have amended the claims to indicate that the genes in other species would be homologs. Support for this amendment is found, for example, page 8, lines 18-29; page 9, lines 20-30 through to page 10, lines 1-24. Therefore, it is apparent from the teachings in the disclosure that the specification provides guidance; one of ordinary skill in the art would not require undue experimentation to make and use the invention with respect to identifying genes from any other fish as per the claims; and the skill in the art required would be one of ordinary skill in the art.

In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

***Claim rejections- 35 U.S.C. § 112-Written Description***

Claims 1-7 and 10-32 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

Applicants respectfully traverse.

The Examiner asserts on page 13, fourth paragraph:

The genus of the claimed invention encompasses substantial variability in the nucleic acid sequences from the different species of fish. The specification fails to provide description or guidance as to which portions of the sequences claimed from the sheepshead minnow and the largemouth bass would be functionally similar in an array for detection in other fish species, such as, salmon or shark. The specification fails to sufficiently describe the claimed invention in clear and exact terms so that a skilled artisan would recognize that the applicants were in possession of the claimed invention at the time of filing.

Applicants respectfully disagree. As discussed by inventor Nancy Denslow in the declaration attached hereto: "Homology does not need to be identical among species of fish. One would identify the genes in other species by using the BLASTP program – as more sequence information is available, these genes would be identifiable in all species. The BLASTP program shows homology with mammalian species as well, thus the similarity would extend to all vertebrates. The homology does not need to be > 90% -- genes are normally found to be homologs because they share high homology in blocks of sequences that are highly conserved and may have low homology in other regions which are of less importance. Thus, one should be able to still identify the homologs and then design specific oligonucleotides based on the sequence of the homologs to test the species of interest."

Applicants also reiterate that the sequences disclosed by Applicants have identified genes which are regulated in response to the estrogenic and/or androgenic agents. Since these genes, see for example Tables I-III, were identified using the SEQ ID NO's disclosed in the instant specification, Applicants submit that the same genes or "homologs" can be identified in any fish species. Further, in order to expedite the prosecution applicants have amended the claims to recite "homologs."

In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

#### ***Claim Rejections Under 35 U.S.C. § 102***

Claims 1-7, 9-24 and 30-32 were rejected under 35 U.S.C. § 102(b) as being anticipated by Larkin et al (Marine Environmental Research 2002 (available online May 24, 2002) Volume 54 p. 395).

Applicants respectfully traverse. However, in order to expedite prosecution Applicants have amended the claims to remove reference to "partially encoded." As such, the cited reference fails to teach each and every claim limitation and therefore, fails to anticipate the instant invention. No new matter has been added by virtue of this amendment and entry is respectfully requested.

In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

#### ***CONCLUSION***

Applicants respectfully request entry of the foregoing remarks and reconsideration and withdrawal of all rejections. It is respectfully submitted that this application with claims 1-32 define patentable subject matter and is in condition for allowance. Accordingly, Applicant respectfully requests allowance of these claims.

If there are any remaining issues or the Examiner believes that a telephone conversation with the Applicants' attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at telephone number shown below.

This response is being filed with a petition for a one month extension of time and the required fee. Although, Applicants believe that no extensions of time or fees are required with submission of this paper, Applicants request that this submission also be considered as a petition for any extensions of time if necessary. The Commissioner for Patents and Trademarks is hereby authorized to charge the amount due for any retroactive extensions of time and any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees paid on the filing or during prosecution of this application to Deposit Account No. 50-0951.

Respectfully submitted,



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Date: January 5, 2007

Docket No. 5853-238